K063744

JAN 17 2007

Special 510(k) Summary

Purpose for Submission

Roche Diagnostics hereby submits this Special 510(k) to provide notification of modification to our Total Bilirubin Special test system. The reagent was originally cleared for use as:

- COBAS INTEGRA Total Bilirubin Special K981632/A001
- And modified as COBAS INTEGRA Total Bilirubin Special K063543

Modifications to the test systems include:

- Reagent application to the **cobas c** 111 analyzer
- Other editorial labeling changes

A full description of the differences and similarities between performance of Total Bilirubin Special on the COBAS INTEGRA 400 plus and **cobas c** 111 is described below.

The **cobas c** 111 analyzer is a new member of the COBAS INTEGRA® family of analyzers and will use reagents and calibrators identical to those of other INTEGRA analyzers. The **cobas c** 111 is a device modification of the current COBAS INTEGRA® 400 plus analyzer, cleared in a letter to file K951595. A full description of the differences and similarities between the two analyzers, software modifications and a summary of the design validation and verification activities for the modified software is included in this submission as part of the modifications to the Total Bilirubin Special test system.

In accordance with the FDA policy, new applications of previously cleared reagents to the **cobas c** 111 analyzer were completed, along with new labeling in the form of **cobas c** 111 package inserts. For all subsequent applications of previously cleared reagents, Roche Diagnostics is following the FDA guidance, *Replacement Reagent and Instrument Family Policy* – Dec 11, 2003, to demonstrate equivalence to the original reagent/instrument performance. Data will be available for FDA review upon request.

The additional labeling provided in this submission is for purposes of CLIA categorization.

Device Name

Proprietary name: **Total Bilirubin Special**

Common name: Bilirubin total

Classification name: Bilirubin (total or direct) test system

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Establishment Registration

The establishment registration number for Roche Diagnostics Gmbh Penzberg is 9610529.

The establishment registration number for Roche Diagnostics Corporation is 1823260.

The establishment registration number for Roche instrument Center (RIC) is 3003795116.

Classification

The FDA has classified a discrete photometric chemistry analyzer in Class I.

Panel	Classification Number	Classification Name	Regulation Citation
75 Clinical Chemistry	CIG	Bilirubin (total or direct) test system	21 CFR 862.1110

Device Description

The Total Bilirubin Special reagent is intended for use on the **cobas c** 111 analyzer for the quantitative determination of total or direct bilirubin in serum and plasma.

The **cobas c** 111 analyzer is a partially automated, *in-vitro* diagnostic analyzer capable of performing clinical chemistry, specific protein and electrolyte tests. Analytes are measured photometrically or turbidimetrically; the analyzer also has an optional ISE module for measuring sodium, potassium and chloride.

The **cobas c** 111 instrument is a random access analyzer designed to be operated on a bench top in the professional environment using a combination of a photometric analysis unit and an optional ion selective electrodes (ISE).

Performance Standards

To date, no performance standards that affect this device have been finalized under Section 514 of the Act.

Intended use

In vitro test for the quantitative determination of total bilirubin in human serum and plasma on the cobas c 111 system.

Predicate device

We claim substantial equivalence to the Total Bilirubin Special reagent cleared as K063543.

Substantial equivalency-Similarities

The table below indicates the similarities and differences between the modified Bilirubin total reagent and its predicate device.

Feature	Modified Device: Total Bilirubin Special	Predicate device: COBAS INTEGRA Total Bilirubin Special, K063543
General		
Intended Use/ Indications for Use	In vitro test for the quantitative determination of total bilirubin in human serum and plasma on the **cobas c** 111 system.	The COBAS INTEGRA Total Bilirubin Special (BILTS) cassette contains an in vitro diagnostic reagent system intended for use on COBAS INTEGRA systems for the quantitative determination of total bilirubin in serum and plasma of adults and neonates (test BILTS, 0-985).
Specimen	serum and plasma	serum and plasma
Test Principle		
Reference method	Same	Diazo method
Reagent information		
Reagent composition	Same	R1: Sodium acetate buffer 85 mmol/L, Sulfamic acid 110 mmol/L R2: Hydrochloric acid 100 mmol/L, Diazonium ion 3 mmol/L
Stability - shelf life and on-board	2-8 °C until expiration date On-board 4 weeks	2-8 °C until expiration date COBAS INTEGRA 400/400 plus: On-board at 10-15 °C 5 weeks COBAS INTEGRA 700/800: On-board at 8 °C 5 weeks

Calibrator	Same	Calibrator f.a.s.
Quality control	Same	Precinorm U, Precipath U Precinorm U plus, Precipath U plus
Traceability	Same	Standardized against the Doumas reference method
Performance characteristics		
Precision	Within-run 1.79% @ 21.7 µmol/L 0.64% @ 64.2 µmol/L 2.94% @ 15.2 µmol/L 0.77% @ 60.0 µmol/L Total 2.32% @ 21.6 µmol/L 0.71% @ 67.4 µmol/L 3.10% @ 16.2 µmol/L 0.79% @ 83.0 µmol/L	Within run: 2.44% @ 15.80 µmol/L 1.39% @ 54.00 µmol/L Between day: 4.13% @ 14.7 µmol/L 2.15% @ 47.20 µmol/L
Measuring range	0.1-25.2 mg/dL 0.1-101 mg/dL (with postdilution)	0-25 mg/dL 0-250 mg/dL (with postdilution)
Lower detection limit	0.1 mg/dL	0.063 mg/dL
Expected values (literature reference)	Same	Adults and children: up to 1.0 mg/dL Neonates: Age of newborn Premature 24hrs: 1.0-6.0 mg/dL 48hrs: 6.0-8.0 mg/dL 3-5 days: 10.0-15.0 mg/dL Age of newborn Full Term 24hrs: 2.0-6.0 mg/dL 48hrs: 6.0-7.0 mg/dL 3-5 days: 4.0-12.0 mg/dL
Endogenous interferences	Same	Hemolysis: No significant interference up to 1000 mg/dL Lipemia: No significant interference up to 1400 mg/dL as Intralipid

Exogenous interferences	Same	Ascorbic acid at 30 mg/dL causes artificially decreased total bilirubin values
Analyzer		
Topic	**cobas c 111 Analyzer (Modified Device)**	**COBAS INTEGRA® 400 plus with ISE (K951595)**
Analyzer Description		
Intended Use	The Roche **cobas c 111** analyzer is an *in-vitro* diagnostic analyzer capable of performing clinical chemistry, specific protein and electrolyte tests. Analytes are measured photometrically or turbidimetrically; the analyzer also has an optional ISE module for measuring sodium, potassium and chloride.	The Roche COBAS INTEGRA 400 plus is an automated in vitro diagnostic analyzer capable of performing general chemistry, specific protein, electrolyte tests, therapeutic drug, drug of abuse and thyroid analyses. It is equipped with modules for absorption photometry, fluorescence polarization photometry and potentiometry (ISE) and works in conjunction with in vitro diagnostic reagents.
Analyzer Description (*continued*)		
Measurement principle	• Absorbance Photometry (enzymes, substrates, proteins) • ISE Potentiometry (electrolytes)	• Absorbance Photometry (enzymes, substrates, proteins, DAT) • Fluorescence Photometry (TDM) • ISE Potentiometry (electrolytes)
Reaction modes	Same	Endpoint, kinetic, potentiometric
Software SIMILARITIES		
Software	cobas c 111 analyzer software	Cobas Integra® 400 plus Analyzer Software
Configuration	Integrated bench top analyzer (including Absorbance Photometer) with optional ISE unit	Integrated benchtop analyzer (incl. Abs, FP-Photometer & ISE module)
Functions performed	Same	Data input, sample processing, result calculation, result reporting, quality control

Computer Infrastructure	Data management & user interaction on embedded CPU with Linux operating analyzer Instrument management and real-time control on embedded CPU with vxWorks operating analyzer	Data management & user interaction on PC based computer with Windows XP operating analyzer Instrument management and real-time control on embedded CPU with vxWorks operating analyzer
Analytical Functions	Same	Control of analytical processes (pipetting, incubation, detection), primary signal processing
Data storage	Same but no patient demographics are stored (due to less storage capacity).	Storage of analyzer and application parameters, calibration data, QC data, sample results, alarms, patient demographics, service actions and status information
Result calculation	Same	Automated measuring of signal for kinetic and endpoint methods according to cycle time and automated calculation of concentration via calibration curve
User management	Same	User ID and password
Flagging of errors	Same	Available
Software DIFFERENCES		
Initial cassette volume check (ICVC) for reagent pipetting	Not applicable: Instead of cassettes single bottles with liquid level detection are used	Available
Data concept (Application parameter transfer)	Applications via barcode	Applications via diskette
Data concept (Cal/QC assigned values)	Automatic QC when QC samples are placed manually	Automatic QC with on board QC samples
Analyzer Features		
Throughput	Max 100 tests per hour	Max 400 tests per hour
Analyzer Size	Same but smaller	Integrated benchtop analyzer
Sample Handling		
Typical sample volumes	Typically 2 - 10 µL per test (same) ISE (serum, plasma): 25 µL (indirect mode) ISE (urine): 25 µL (indirect mode):	Typically 2 - 10 µL per test ISE (serum, plasma): 20 µL (indirect mode) 97 µL (direct mode) ISE (urine): 20 µL (indirect mode):

Sample Types	Same, but not CSF	Serum, plasma, urine, CSF; whole blood and hemolysate for HbA1c
Sample Handling Analyzer	Sample area for samples, calibrators and controls.	Rack analyzer for samples, calibrators and controls.
Sample capacity on board	8 places for cups / tubes.	Up to six racks with max. 15 sample cups/tubes per rack on board.
Sample identification	Same	1D- Barcode
Reagent Handling		
Reagent Volume	Same	20 – 150 µL
Reagent Container	Unisys 20mL bottle	Integra cassette / cobas c pack
Reagent Container (Electrolytes)	Same	Plastic bottles closed with screwcaps
Reagent Access	Manual opening of bottle prior to placement on board	Reagent cassette caps pierced automatically inside the instrument.
Onboard storage temperature	Refrigerated 6-10 °C (43-50 °F)	Refrigerated 10 - 15 °C (50-59 °F)
Reagent bottle/cassette identification	Same	Barcode
On board reagent storage capacity	27 reagent bottles	32 cassettes
Analyzer cycle time	18 sec	10.6 sec
Reagent mixing	Stirring in cuvette with steel probe	Integrated cuvette vortex mixer
Auto rerun	Manual only	Available
Pipetting Analyzer		
Sample and reagent syringes	XZ-Phi robotic syringe	XYZ robotic syringe
Reagent probes	1 polished steel probe with modified design (used for sample & reagent)	2 polished steel probes (used for sample & reagent)
Sample probes	1 polished steel probe with modified design (used for sample & reagent)	2 polished steel probes (used for sample & reagent)
Probe cleaning	Same	Automatic incl. carry over evasion
Liquid level detection	Same (+ reagent pipetting)	Both probes conductance for sample pipetting
Clot detection	Not available	Available – pressure sensor

Test Reaction Chamber		
Temperature Control	Same	Heated air bath 37 °C (99 °F)
Cuvettes	Same	PMMA acrylic plastic – for single use
ISE Module		
ISE Module	Serum, plasma indirect (1:6 dilution) Urine indirect (1:6 dilution) One-point calibration every sample measurement.	Serum, plasma direct (undiluted) Serum, plasma indirect (1:6 dilution) Urine indirect (1:6 dilution) One-point calibration every sample measurement.
Ion Selective Electrodes	Same but no lithium electrode	Potentiometric: chloride, potassium, sodium, lithium and reference electrode
ISE throughput	60 samples / h	66 samples / h
Detection Information		
Spectrophotometer	Same	Grating monochromator and diode array
Light source	Tungsten / Halogen lamp, 20 W	Tungsten / Halogen lamp, 100 W
Light path	Same	5 mm path length
Measuring unit	Same	Intensity (0 - 2.0 A)
Wavelengths	340, 378, 409, 449, 480, 512, 520, 552, 583, 629, 652, 659 nm mono- and bichromatic measurements	340, 378, 409, 480, 512, 520, 552, 583, 629, 652, 659, 800 nm mono- and bichromatic measurements
Calibration and quality control		
Calibrators	Same	Multiple use
Calibration modes	Same	Linear, non linear. Multiple standards. Generation of multipoint standard curves by automatic dilution.
Calibration / on board stability	Same	Typically each lot or 12 weeks for same reagent on board
Control storage on instrument	To be placed on demand	Within sample area possible
Calibrator / control value transfer	Same	Via barcode transfer sheet or manual entry
Internal quality management analyzer	Same	Available to monitor and validate test results
Interfaces		
Host interface	Same	RS232C bi-directional

Printer	Internal thermo paper printer	Standalone LaserJet type
Display	Internal LCD touch panel (1/4 VGA size)	Standalone 17" computer display w. keyboard and mouse

Proposed Labeling

Total Bilirubin Special reagent:
Proposed labeling sufficient to describe the device, its intended use, and the directions for use can be found in the separately attached document. We believe the proposed version of the device labeling presented contains all of the technical information required per 21 CFR 809.10.

cobas c 111 analyzer:
Draft **cobas** c111 method manual sheets and example cassette labels for CLIA categorization purposes in this submission.

A complete User's Manual for the **cobas** c111 analyzer is provided in **Volume II** of this submission.

A CD-ROM containing the COBAS INTEGRA 400 plus Operator's Manual (the predicate device for **cobas c** 111 analyzer) is included with this submission.

We believe the proposed version of the device labeling presented contains all of the technical information required per 21 CFR 809.10.

Validation and Design Control

Development activities were conducted under appropriate design control procedures and the overall product specifications were met. The Results of Risk Analysis and Declaration of Conformity with Design Controls are provided with this submission.

Confidentiality

Roche Diagnostics requests that the FDA not disclose the nature or existence of this submission until the substantial equivalence decision has been reached.

Closing

Modification of the Bilirubin Total reagent does not affect the intended use or indications for use of the device as described in the labeling, nor does it alter the fundamental scientific technology of the device. Therefore, we trust the information provided in this Special 510(k) will support a decision of substantial equivalence to its predicate for the Total Bilirubin Special application to **cobas c** 111 analyzer.

An electronic copy (scanned pdf version) of this submission can be provided upon request. If you have any questions or require further information, please do not hesitate to contact this office.

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Sincerely,

Corina Harper, RAC
Regulatory Affairs Consultant
Roche Diagnostics Corporation

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Roche Diagnostics
9115 Hague Road
Indianapolis, IN 46250
Attn: Corina Harper

JAN 17 2007

Re: k063744
Trade/Device Name: Total Bilirubin Special
Regulation Number: 21 CFR §862.1110
Regulation Name: Bilirubin (total or direct) test system.
Regulatory Class: Class II
Product Code: CIG
Dated: December 15, 2006
Received: December 18, 2006

Dear Ms. Harper:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at (240) 276-0490. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address at http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Jean M. Cooper, M.S., D.V.M.

Jean M. Cooper, M.S., D.V.M.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K063744

Device Name:
Total Bilirubin Special

Indications For Use:

In vitro test for the quantitative determination of total bilirubin in human serum and plasma on the cobas c 111 system.

Measurements of the levels of bilirubin and organic compound formed during normal and abnormal destruction of red cells, is used in the diagnosis of liver, hemolytic hematological and metabolic disorders, including hepatitis and gall bladder block.

Prescription Use ___XXX____ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Carol C. Benson
Division Sign-Off

Office of In Vitro Diagnostic Device
Evaluation and Safety

K063744